



https://doi.org/10.47660/CBR.2020.17470

# BIOLOGICAL THERAPY EVEN AFTER WASHED OUT DECREASES IMMUNE RESPONSE OF YELLOW FEVER PRIMARY VACCINATION IN SPONDYLOARTHRITIS

Thays Zanon Casagrande<sup>1,\*</sup>, Ketty Lysie Libardi Lira Machado<sup>1</sup>, Samira Tatiyama Miyamoto<sup>1</sup>, Arthur Dalmaso Pinto<sup>1</sup>, Priscila Costa Martins Rocha<sup>1</sup>, Erica Vieira Serrano1, Valquiria Garcia Dinis<sup>1</sup>, Sônia Alves Gouvêa<sup>1</sup>, João Gabriel Fragoso Dias<sup>1</sup>, Maria Bernadete Renoldi de Oliveira Gavi<sup>1</sup>, Lidia Balarini da Silva1, Ruben Horst Duque<sup>1</sup>, Ana Paula Espíndula Gianordoli<sup>1</sup>, Karine Gadioli Oliveira<sup>1</sup>, Lauro Ferreira da Silva Pinto-Neto<sup>4</sup>, Elizandra Tomazela Laurenti Polito<sup>5</sup>, Leticia Resende Brandão<sup>5</sup>, Sheila Maria Barbosa de Lima<sup>3</sup>, Emily Hime Miranda<sup>3</sup>, Gisela Freitas Trindade<sup>3</sup>, Maria de Lourdes de Sousa Maia, Ana Carolina Campi-Azevedo<sup>2</sup>, Andréa Teixeira-Carvalho<sup>2</sup>, Vanessa Peruhype-Magalhães<sup>2</sup>, Ismael Artur da Costa-Rocha<sup>2</sup>, Olindo Assis Martins-Filho<sup>2</sup>, Valéria Valim<sup>1</sup>

1. Universidade Federal do Espírito Santo, Vitória (ES), Brazil. 2. Fundação Oswaldo Cruz, Belo Horizonte (MG), Brazil. 3. Fundação Oswaldo Cruz, Rio de Janeiro (RJ), Brazil. 4. Santa Casa de Misericórdia, Vitória (ES), Brazil. 5. Sociedade de Reumatologia do Espírito Santo, Vitória (SE), Brazil.

\*Corresponding author: thays.zanon@gmail.com

## BACKGROUND

Yellow fever (YF) vaccination might cause a large number of adverse events (AE) and suboptimal responses in patients with autoimmune diseases (AID); however, there have been no studies on 17DD-YF primary vaccination performance in spondyloarthritis group. Those patients are younger and have less comorbidities than other AID patients and frequently receive biological therapy, which is known to reduce immune response.

### **MATERIALS AND METHODS**

Prospective non-interventional study accomplished in 2017 assessing safety and immunogenicity of planned 17DD-YF primary vaccination. Adult patients with spondyloarthritis (SpA, n = 51) were enrolled along 38 healthy controls (HC), referred for planned vaccination by a rheumatologist. All had low level immunosuppression or had their biological therapy washed out for a period of five half-lives before vaccination. The occurrence of AE, neutralizing antibody kinetics, seropositivity rates and 17DD-YF viremia were evaluated at various time points [day 0 (D0), D3, D4, D5, D6, D14, and D28], BASDAI scores were evaluated at D0 and D180.

#### RESULTS

Only mild AEs were reported at D28, incidence of local and systemic AEs was similar between SpA and HC groups (4 vs. 8% and 26 vs. 21%; p = 0.65 and 0.8, respectively). The SpA group presented late seroconversion profiles according to the plaque reduction neutralization test (PRNT) related to HC (28 vs. 78% in D14 and 73 vs. 96% at D28,  $p \le 0.001$ ). Plaque reduction neutralization test titers in the HC group were 440 HC 95% (291–665), higher than in the SpA group 112 (73–170, p < 0.001). (Fig. 1 - PRNT titers and seropositivity in SpA and HC). The peak of YF viremia was at D5, with a similar number of copies in both groups (8.2 ± 0.7 × 10<sup>3</sup> copies/mL in the HO group vs 11.3 × 103 EAp, p = 0.56). In SpA subgroup (Bio and nonBio) analyses, previous biological therapy leads to lower PRNT (Bio 79, 95% CI [39–150] vs. nonBio 159, 95% CI [94–267], p < 0.001). The nonBio group achieved a similar response to the HC group (81 vs. 96%, p = 0.112), whereas the Bio group had a lower seroconversion rate (64 vs. 96% HC, p = 0.007). (Fig. 2 - PRNT titers and seropositivity in SpA subgroups).



Figure 1. Plaque reduction neutralization test titers and seropositivity in SpA and HC.



Figure 2. Plaque reduction neutralization test titers and seropositivity in SpA subgroups.

#### CONCLUSION

The 17DD YF vaccine is safe for SpA patients, even with previous biological therapy. Those patients have low levels of antibodies and low seroconversion rate, suggesting the need for a longer biological therapy pause for immune reconstitution.